

Thomas J. Meade, Ph.D. Departments of Chemistry, Biochemistry, Cell Biology Molecular Biology & Neurobiology and Physiology Northwestern University Evanston, IL 60208-3113 (847)-491-2481

Education

<u>Postdoctoral Research Fellow</u>. California Institute of Technology, 1987-89. Advisor: Professor Harry B. Gray.

National Institutes of Health Postdoctoral Fellow. Harvard Medical School and the Massachusetts General Hospital, 1985-1987. Advisor: Professor Thomas J. Brady.

<u>Ph.D.</u> in Inorganic Chemistry, The Ohio State University; Columbus, Ohio, August, 1985. Dissertation Advisor: Professor Daryle H. Busch.

M.S. in Chemistry (Division of Biochemistry), The Ohio State University, Columbus Ohio, 1982. Thesis Advisor: Professor Perry A. Frey.

<u>B.S.</u> with Honors in Chemistry, Arizona State University; Tempe, Arizona, May, 1980. Honors Thesis Advisor: Professor Therald Moellar.

Professional Experience

Professor of Chemistry; Biochemistry and Molecular and Cell Biology and Neurobiology and Physiology; Northwestern University (2002-)

Senior Research Faculty, Division of Biology and the Beckman Institute, California Institute of Technology, (1996-2002).

Research Faculty: Div. of Biology, California Institute of Technology, (1991-96).

Research Interests

Chemistry of Life Sciences, bioinorganic chemistry and biological imaging with particular emphasis on:

INORGANIC CHEMISTRY- Design, synthesis and physical properties of coordination complexes, including systems incorporating novel functionality for magnetic resonance and fluorescence imaging of biological systems.

ELECTRON TRANSFER MECHANISMS- Investigate long-range electronic coupling through stacked, π -unsaturated systems, conducting biopolymers and the development of biosensors.

BIOLOGICAL MICROSCOPY- Design and synthesis of spectroscopic and magnetic probes for *in vivo* microscopic imaging of nerve patterning, regulation of cell lineage, gene expression and DNA transfection.

METAL COMPLEXES AS ENZYME INHIBITORS- Investigate the interaction of small-molecule transition metal complexes as enzyme inhibitors for the development of therapeutic antitumor and antiviral drugs.

Honors and Awards

National Academy of Engineering Lecturer, Cleveland, Ohio, 2000.

Pendergast Lecturer, University of Pennsylvania, 1999.

American College of Neuropharmacology Lecturer, 1999.

Grubstakes Award, Direct Detection of Gene Expression via Magnetic

Resonance Imaging; Caltech, 1996, 1998.

Watson Lecturer, Caltech, 1997.

NIH Postdoctoral Research Fellow, 1986.

National Research Service Award, Harvard Medical School, 1985.

Ohio State University Teaching Award (student selected), 1981.

B.S. with Honors Thesis, 1980.

Professional Service

Editorial Advisory Board: Inorganic Chemistry; 1999-

Program Workshop Chair, CTEP drug development program,

National Cancer Institute; 1999-2000.

Editorial Advisory Board: Bioconjugate Chemistry; 1999-.

Ad hoc member; NIH Metallobiochemistry Study Section; 1999-.

Chairmen: Imaging in 2020; National Cancer Institute; 1999-2001.

Founder and SAB Member, Metaprobe Inc. Pasadena, CA. 1998-present.

Chairmen: After The Genome IV Conference; 1998.

Guest Editor: Coordination Chemistry Review, 1998-99.

Cofounder and Scientific Advisory Board Member, Clinical Micro Sensors Inc.,

Pasadena, CA. 1995-present.

11 named and 62 Invited lectures; 1992-2002.

Teaching

Supervised undergraduate and graduate laboratories and led recitation sections (O.S.U. 1980-81). Ohio State University Teaching Award (student selected) 1981.

Codirector and Founder; "Seeing is Believing: A Classroom Tour of the Sciences." Pasadena Unified School District and local private schools, 1994-

Affiliations

American Chemical Society, American Association for the Advancement of Science, International Society for Magnetic Resonance in Medicine, Sigma Chi Honorary Research Society, Alpha Chi Sigma, New York Academy of Sciences, Society for Molecular Imaging.

Trainee History

Supervised 16 undergraduates, 16 graduate students and 14 post-doctoral fellows, 1992-present.

Publications

- Meade, T.J., Iyenger, P.A., Frey, P.A., "Synthesis and Rearrangements of Alkyl Phosphorothioates", <u>Journal of Organic Chemistry</u>, 1985, 50, 936.
- Meade, T.J., Busch, D.H., "Inclusion Complexes of Molecular Transition Metal Hosts", Progress in Inorganic Chemistry, Stephen J. Lippard, Ed., 1985, 33, 59-127.
- Goldsby, K., Meade, T.J., Kojima, M., Busch, D.H., "¹³C NMR Spectroscopy as a Probe of the Exclusively Steric Effects of Ligand Superstructure on the Binding Constants of Lacunar Macrobicyclic Complexes with Dioxygen", <u>Inorganic Chemistry</u>, 1985, 24, 2588.
- Meade, T.J., Kwik, W.L., Herron, N., Alcock, N.W., Busch, D.H., "Hydrophobic, Regiospecific Guest Binding by Transition Metal Host Complexes Having Permanent Voids as Revealed by FT-NMR Relaxation Studies", <u>Journal of the American Chemical Society</u>, 1986, 108 1954.
- Chavan, M.Y., Meade, T.J., Busch, D.H., Kuwana, T., "Structural Dependence of an Electron-Transfer Process: Nature of the Products of a One Electron Oxidation of the Lacunar Cyclidene Complexes of Nickel(II) and Cobalt(II)", <u>Inorganic Chemistry</u>, **1986**, 25, 314.
- Meade, T.J., Takeuchi, K.J., Busch, D.H., "A Highly Novel Inclusion Complex Containing the Dioxygen Molecule and an Organic Guest Molecule Cohabitating within a Vaulted Cobalt(II) Cyclidene Host", <u>Journal of the American Chemical Society</u>, **1987**, 109, 725.
- Cameron, J.H., Kojima, M., Korybut-Daszkiewicz., Coltrain, B.K., Meade, T.J., Alcock, N.W., Busch, D.H., "Inclusion Complexes Involving a Novel Ligand Superstructure-Dioxygen Adducts and other Derivatives of Retro-Bridged Cyclidene Iron, Cobalt, and Nickel Complexes", Inorganic Chemistry, 1987, 26, 427.
- Meade, T.J., Fendrick, C.A., Podalick, P.E., Cotrell, C.E., Busch, D.H., "Elucidation of Structural Relationships and Assignment of the ¹H NMR Spectra of Several Transition Metal Cyclidene Complexes using 2-D NMR", <u>Inorganic Chemistry</u>, 1987, <u>26</u>, 4252.
- Lauffer, R.B., Vincent, A.C., Padmanabhnm S., Meade, T.J., "Sterospecific Binding of Racemic-Iron(III) N.N'-Ethylenebis[(5-bromo-2-hydroxyphenyl)-gylcinate] to the Bilirubin Site on Human Serum Albumin", <u>Journal of the American Chemical Society</u>, **1987**, 109, 1622.
- Meade, T.J., Bowler, B.E., Gray, H.B., "Recent Advances in Long-Range Electron Transfer in Biological Systems", <u>McGraw-Hill Yearbook of Science and Technology</u>, McGraw-Hill Book Company: New York, Vol. 11, 53, 1989.
- Meade, T.J., Winkler, J. R., Gray H.B., "Driving-Force Effects on the Rate of Long-Range Electron Transfer in Ruthenium-Modified Cytochrome c", <u>Journal of the American</u> Chemical Society, 1989, 111, 4353.

- Bowler, B.E., Meade, T.J., Mayo, S.L., Richards, J., Gray, H.B., "Electron Transfer in Structurally Engineered Metalloproteins.", <u>Journal of the American Chemical Society</u>, **1989**, 111, 8757.
- Meade, T.J., Alcock, N.W., Busch, D.H., "Inclusion Complex Formation Involving a New Class of Transition-Metal Host", <u>Inorganic Chemistry</u>, 1990, 29, 3766.
- Risser, S.M., Beratan, D.N., Meade, T.J., "Electron Transfer in DNA: Predictions of Both Exponential Growth and Decay of Coupling with Distance.", <u>Journal of the American Chemical Society</u>, <u>115</u>, 2508, **1993**.
- Meade, T.J., Jacobs, R.E., Fraser, S.E., "The Design and Synthesis of Magnetic Resonance Imaging Agents for Embryonic Cell Lineage Analysis." <u>Journal of Inorganic</u> Biochemistry, 51, 118, 1993.
- Meade, T.J., "Covalent Attachement of Electron Donor-Acceptor Pairs to DNA." <u>J. Polym. Sci. Part A. Polym. Chem.</u>, <u>32</u>, **1994**.
- Meade, T.J., Kayyem, J.F., "Electron Transfer Through DNA: Site-Specific Modification of Duplex DNA with Ruthenium Donors and Acceptors." <u>Angew. Chem. Int. Ed. Engl.</u>, 34, 352, 1995. Angew. Chem. (Ger.) 107, 358, 1995.
- Kayyem, J.F., Kumar, R., Fraser, S.E., Meade, T.J., "Receptor Targeted Co-Transport of DNA and Magnetic Resonance Contrast Agents" <u>Chemistry and Biology</u>, **1995**, <u>2</u>, 615-620.
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- Meade, T.J., "Electron Transfer Through the DNA Double Helix," Metal Ions in Biological Systems, (A. Sigel, H. Sigel, eds.) Vol. 32., Chapter 13, 1996, 453-478.
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- Alcock, N.W., Busch, D.H., Chmielewski, Coltrain, B.K., Meade, T.J., "Structures of the Multireceptor Vaulted Cyclidene Complexes." <u>Inorg. Chimca Acta.</u>, 1996, 246, 109-118.
- Moats, R.M., Fraser, S.E., Meade, T.J., "A *Smart* Magnetic Resonance Imaging Contrast Agent That Reports on Enzymatic Activity," <u>Angew. Chem. Int. Ed. Engl.</u> 1997, 36, 726.
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- Meade, T.J., Kayyem, J., Noy, A., Lieber, C.M., "Mechanics and Energetics of Binding in DNA Studied by Chemical Force Microscopy." Chemistry and Biology. 1997, 4, 519.

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- Louie, A., Meade, T.J., "A Cobalt Complex That Selectively Disrupts the Structure and Function of Zinc Finger Proteins." <u>Proc. Natl. Acad. Sci.</u> USA, **1998**, <u>95</u>, 6663-6668.
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- Takeuchi, T., Bottcher, A., Quezda, C., Simon, M., Gray, H.B., Meade, T.J., "Selective Inhibition of Human □-Thrombin by Cobalt(III) Schiff Base Complexes." <u>Journal of the American Chemical Society</u>, 1998, 120, 8555-8556.
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- Li, W.H., Fraser, S.E., Meade, T.J. "A Calcium Sensitive Magnetic Resonance Imaging Contrast Agent." <u>Journal of the American Chemical Society</u>, **1999**, <u>121</u>, 1413-1414.
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- Meade, T.J., Louie, A., Jacobs, R.E., Fraser, S.E., "Biochemically Activated Magnetic Resonance Imaging Agents." <u>Biomarkers and Surrogate Endpoints: Clinical Research and Applications</u>. Elsevier, International Congress Series, Amsterdam, **2000**.
- Louie, A., Huber, M., Ahrens, E., Jacobs, R.E., Fraser, S.E., Meade, T.J., "In-vivo Visualization of Gene Expression by Magnetic Resonance Imaging." <u>Nature Biotechnology</u>, **2000**, <u>18</u>, 321-325.
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Oligonucleotides: Unexpected Cyclization Reaction of the Uridine Base." <u>Journal of the American Chemical Society</u>, **2000**, *122*, 6767-6768.

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Meade, T.J., "Seeing is Believing." Academic Radiology, 2000, 8, 1-3.

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Yu, C.J., Yanjian Wan, Y., Li, J., Yowanto, H., Donilon, L.H., Tao, C., Blackburn, G.F., Meade, T.J., "Electronic Detection of Single Base Mismatches in DNA using Ferrocene-Modified Probes." Journal of the American Chemical Society, 2001, 123, 11155-11161.

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Li, W., Giacomo, P., Fragai, M., Luchinat, C., Meade, T.J., "H¹ Mechanistic Studies and NMR Structure of a Calcium Sensitive MR Contrast Agent." <u>Inorganic Chemistry</u>, **2002**, *41*, 4018-4024.

Louie, A., Dumistra, J., Meade, T.J., "Mapping Gene Expression by MRI" in <u>BRAIN</u> MAPPING: The Methods, Elsevier Science (USA) (J. Mazziota, A. Toga ed). **2002**, 819-828.

Modo, M., Cash, D., Mellodew. K., Steven C.R. Williams. SCR., Fraser, S.E., Meade, T.J., Price, J., Hodges, H., "Tracking transplanted stem cell migration using bifunctional, contrast agent-enhanced, magnetic resonance imaging." <u>Neuroimage</u>, **2002** *17*, 803-811.

Frank, N., Meade, T.J., "Donor-Acceptor Modification of Oligonucleotides with High and Low Potential Transition Metal Complexes." <u>Inorganic Chemistry</u>, **2002**, in press.

Patents

Meade, T.J., "Synthesis of Aromatic Heterocyclic Polymers from a Biosynthetically Prepared Precursor." U.S. Patent Number-5,340,913 (1992).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-5,591,578 (1997).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Direct Detection of Nucleic Acids by Electron Transfer Mechanisms." U.S. Patent Number-5,705,348 (1997).

Meade, T. J., Fraser, S.E., Jacobs, R.E., "Magnetic Resonance Imaging Agents for the In Vivo Detection of Physiological Processes." U.S. Patent Number- 5,707,605, (1997).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Amperometric DNA Hybridization Detection by Electron Transfer Reactions." U.S. Patent Number-5,770,369 (1998).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-5,780,234 (1998).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer: Single vs. Double Stranded." U.S. Patent Number-5,824,473 (1998).

Grinstaff, M.W., Gray, H.B., Meade, T.J., "Metal Complexes as Cysteine Protease Inhibitors." U.S. Patent Number-5,880,149 (1999).

Meade, T.J. Fraser, S.E., Jacobs, R.E., "Bifunctional Detection Agents Having a Polymer Covalently Linked to a MRI Agent and an Optical Dye." U.S. Patent Number-5,900,228 (1999).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-5,952,172 (1999).

Meade, T.J. Fraser, S.E., Jacobs, R.E., Li, Wenhong, "Magnetic Resonance Imaging Agents for the Detection of Physiological Agents." U.S. Patent Number-5,980,862 (1999).

Meade, T.J., Takeuchi, T., Gray, H.B., Simon, M.I., Louie, A.Y., "Cobalt Schiff Base Compounds." U.S. Patent Number-6,008,190 (1999).

Meade, T.J., "Detection of Analytes Using Reorganization Energy" U.S. Patent Number-6,013,170 (2000).

Meade, T.J., "Direct Detection of Analytes" U.S. Patent Number-6,013,459 (2000).

Meade, T.J., Fraser, S.E., Kayyem, J.F., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,087,100 (2000).

Meade, T.J., Kayyem, J.F., "Methods of Attaching Conductive Oligomers to Electrodes." U.S. Patent Number-6,090,933 (2000).

Kayyem; J.F., O'Connor, S., D., Gozin, Yu, C.J., Meade. T.J., "Electrodes Linked via Conductive Oligomers to Nucleic Acids." U.S. Patent Number-6,096,273 (2000).

Meade, T.J., Fraser, S.E., Jacobs, R.E., "Bifunctional detection agents having an optical dye linked to an MRI contrast agent." U.S. Patent Number-6,123,921 (2000).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,177,250 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,180,352 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,200,761 (2001).

Kayyem; J.F., O'Connor, S., D., Gozin, Yu, C.J., Meade. T.J., "Methods of Detecting Nucleic Acids Using Electrodes." U.S. Patent Number-6,221,583 (2001).

Kayyem, J. F., Meade, T.J., Fraser, S.F., "Cell-Specific Contrast Agent and Gene Delivery Vehicles." U.S. Patent Number-6,232,295 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,238,870 (2001).

Meade, T.J. "Detection of Analytes Using Reoganization Energy." U.S. Patent Number-6,248,229 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,258,545 (2001).

Blackburn, G., Creager; S.E., Fraser; S., Bruce D., Meade; T. J., O'Connor, S.D., Terbrueggen; R.H., Vielmetter, J.G., Welch; T., "Binding acceleration techniques for the detection of analytes." U.S. Patent Number-6,264,825 (2001).

Meade, T.J., Kayyem, J.F., "Metallic Solid Supports Modified with Nucleic Acids." U.S. Patent Number-6,265,155 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,268,149 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,268,150 (2001).

Meade, T.J., Kayyem, J.F., Fraser, S.E., "Nucleic Acid Mediated Electron Transfer." U.S. Patent Number-6,277,576 (2001).

Meade, T.J., Kayyem, J.F., "Metallic Solid Supports Modified with Nucleic Acids." U.S. Patent Number-6,291,188 (2001).

Meade, T.J., Welch, T.W., "Nucleosides Comprising Polydentate Ligands." U.S. Patent Number-6,444,423 (2002).

Pending Applications: 24

Scientific Press

Chemical and Engineering News, "DNA 2001

Scientific American, "Gene Scenes: New MR Imaging Lights Up When DNA Turns On." 2000, 283 (2), 20.

Analytical Chemistry, "Science: MRI for Gene Expression." Zubritsky, Elizabeth. 2000, 320, 319-320.

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<u>Science</u>, "Magnetic Resonance Imaging Detecting Enzyme Activity in Live Animals (News of the Week)." Strauss, Evelyn. **2000**, *287*, 1575.

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<u>Chemical and Engineering News</u>, "Imaging in 2020: Seeing is Believing (Science/Technology)." Ritter, Stephen K. 1999, 77, 30-35.

<u>Chemical and Engineering News</u>, "MRI Contrast Agent Has Eyes Only For Calcium (Science/Technology)." Brennan, Mairin. 1999, 77, 36.

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<u>Chemical and Engineering News</u>, "DNA's Conductance Still Confounds: New Experiments Improve Data, But Don't Resolve Question of Distance-Dependent Electron Migration (Science/Technology)." Wilson, Elizabeth K. **1998**, *76*, 51-54.

<u>Chemical and Engineering News</u>, "Instant DNA Detection: Systems Based on Electrical Signals Move from Science to Reality (Science/Technology)." Wilson, Elizabeth K. 1998, 76, 47-49.

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New Scientist, "Switched On: Molecular Cages Catch Genes in the Act (This Week)." Guterman, Lila. 1998, 159, 7.

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<u>Trends in Biotechnology</u>, "The Development of In Vivo Imaging Systems to Study Gene Expression (Focus)." Bogdanov, Alexei Jr. and Weissleder, Ralph. 1998, 16, 5-10.

<u>Chemical and Engineering News</u>, "DNA: Insulator or Wire? Flurry of New Research, Heated Debate Focuses on Biomolecule (Science/Technology)." Wilson, Elizabeth K. **1997**, 75, 33-39.

<u>Chemical and Engineering News</u>, ""Smart" Imaging Agent is Activated by Enzyme (News of the Week)." Borman, Stu. **1997**, *75*, 13.

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<u>The Economist</u>, "Genetic Screening: Integrated Circuit (Science and Technology)." 1995, 334, 85.